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M PTO-1449 and B (Modified)	APPLICATION NO.: 09/982,548	ATTY. DOCKET NO.: M0656/7070
INFORMATION DISCLOSURE	FILING DATE: October 18, 2001	
STATEMENT BY APPLICANT	APPLICANT: Liu et al.	
Chart I I	GROUP ART UNIT: 1623	EXAMINER: Unassigned

## U.S. PATENT DOCUMENTS

Examiner's Cite	U.S. Patent Document		Name of Patentee or Applicant of Cited	Date of Publication or of issue		
Initials#	No.	Number	Kind Code	Document	of Cited Document MM-DD-YYYY	
	Al	4,281,108	Bl	Fussi	07/28/1981	
	A2	4,341,869	BI	Langer, Jr. et al.	07/27/1982	
	A3	4,373,023	BI	Langer et al.	02/08/1983	
	A4	4,396,762	BI	Langer et al.	08/02/1983	
	A5	4,443,545	BI	Langer, Jr. et al.	04/17/1984 H	
	A6	4,745,105	BI	Griffin et al.	05/17/1988	
	A7	4,757,056	BI	Van Gorp et al.	07/12/1988 9 5 07/17/1990 9 6	
	A8	4,942,156	BI	Foley et al.	07/17/1990	
	A9	4,990,502	B1	Lormeau et al.	07/12/1988 88 9 07/17/1990 2/05/1991	
	A10	5,010,063	BI	Piani et al.	04/23/1991	
	A11	5,039,529	B1	Bergendal et al.	08/13/1991	
	A12	5,106,734	B1	Nielsen	04/21/1992	
	A13	5,152,784	BI	Tsilibary	10/06/1992	
	A14	5,164,378	BI	Conti et al.	11/17/1992	
	A15	5,169,772	BI	Zimmerman et al.	12/08/1992	
	A16	5,204,323	BI	Findlay et al.	12/08/1992	
	A17	5,252,339	BI	Cristofori et al.	10/12/1993	
	A18	5,262,325	BI	Zimmermann et al.	10/12/1993	
	A19	5,290,695	Bi	Morikawa et al.	03/01/1994	
	A20	5,338,677	B1	Zimmermann et al.	08/16/1994	
	A21	5,389,539	BI	Sasisekharan et al.	02/14/1995	
	A22	5,474,987	BI	Cohen et al.	12/12/1995	
	A23	5,567,417	Bl	Sasisekharan et al.	10/22/1996	
	A24	5,569,600	BI	Sasisekharan et al.	10/29/1996	
	A25	5,576,304	Bl	Kakkar et al.	11/19/1996	
	A26	5,599,801	Bl	Branellec et al.	02/04/1997	
	A27	5,618,917	Bl	Toback et al.	04/08/1997	
	A28	5,619,421	B1	Venkataraman et al.	04/08/1997	
_	A29	5,681,733	BI	Su et al.	10/28/1997	
	A36	5,714,376	BI	Sasisekharan et al.	02/03/1998	
	A31	5,744,515	BI	Clapper	04/28/1998	
	A32	5,753,445	BI	Fillit et al.	08/12/1998	
	A33	5,763,427	BI	Weitz et al.	06/09/1998	
	A34	5,776,434	BI	Purewal et al.	07/07/1998	
	A36	5,795,875	BI	Holme et al.	08/18/1998	
	A36	5,808,021	BI	Holme et al.	09/15/1998	
	A37	5,824,299	BI	Luster et al.	10/20/1998	

	ga);				ᆏ
	38 830,726	- B1	Sasisekharan et al.	11/03/1998	오
V. 134	5,855,913	B1	Hanes et al.	01/05/1999	<u>8</u> 8
	40 5,874,064	B1	Edwards et al.	02/23/1999	==
Α.	41 5,879,713	Bl	Roth et al.	03/09/1999	<u> </u>
A	42 5,919,693	Bl	Su et al.	07/06/1999	- market
· A	43 5,922,358	BI	Doutremepuich et al.	07/13/1999	1,600/
A	44 5,968,822	Bl	Pecker et al.	10/19/1999	290
A	45 5,985,309	Bl	Edwards et al.	11/16/1999	8
A	46 5,997,863	Bl	Zimmermann et al.	12/07/1999	
A	47 6,013,628	Bl	Skubitz et al.	01/11/2000	
A	48 6,116,237	B1	Schultz et al.	09/12/2000	
A	49 6,136,295	B1	Edwards et al.	10/24/2000	
A	50 RE37,053	BI	Hanes et al.	02/13/2001	
A	51 6,217,863	Bl	Godavarti et al.	04/17/2001	

Examiner's Initials#	Cite	For	eign Patent Docu	ıment	Name of Patentee or Applicant of Cited	Date of Publication of	Translation
		No.	Office/ Country	Number	Kind Code	Document (not necessary)	Cited Document MM-DD-YYYY
	BI	EP	0 433 225	A1	CIBA-GEIGY AG	06/19/1991	
	B2	wo	93/08289	A1	Massachusetts Institute of Technology	04/29/1993	_
	B3	EP	0 557 887	A2	OPOCRIN S.p.A.	09/01/1993	7
	B4	WO	93/19096	A1	Cancer Research Campaign Technology	09/30/1993	
	B5	wo	94/21689	Al	Cancer Research Campaign Technology	09/29/1994	2 2
	B6	WO	95/34635	Al	IBEX Technologies	12/21/1995	Ш ні,
	B7	wo	97/16556	Al	Massachusetts Institute of Technology	05/09/1997	O ≈
	B8	WO	00/12726	A2	Massachusetts Institute of Technology	03/09/2000	T 4
	B9	WO	00/65521	A2	Massachusetts Institute of Technology	11/02/2000	~

OTHER ART - NON PATENT LITERATURE DOCUMENTS

Examiner's Initials#	Cite No	Include name of the author (in CAPITAL LETTERS) title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, relevant page(s), volume-issue number(s), publisher, city and/or country where published.	Translation (Y/N)
Ci		ALDERMAN, C.P. et al., "Continuous Subcutaneous Heparin Infusion for Treatment of Trousseau's Syndrome", The Annals of Pharmacotherapy, July/August 1995, Pages 710-713, Vol. 29	
	C2	BERNSTEIN, H. et al., "Immobilized Heparin Lyase System for Blood Deheparinization", Methods in Enzymology, 1988, Pages 515-529, Vol. 137, Academic Press, Inc.	
	C3	CARDIN, A.D. et al., "Molecular Modeling of Protein-Glycosaminoglycan Interactions", Arteriosclerosis, January/February 1989, Pages 21-32, Vol. 9, No. 1	
	C4	COMFORT, A.R. et al., "Immobilized Enzyme Cellulose Hollow Fibers: III. Physical Properties and <i>In Vitro</i> Biocompatibility", <i>Biotechnology and Bioengineering</i> , 1989, Pages 1383-1390, Vol. 34, John Wiley & Sons, Inc.	
	C5	EDWARDS, D.A. et al., "Large Porous Particles for Pulmonary Drug Delivery", Science Reprint Series, June 20, 1997, Pages 1868-1871, Vol. 276, American Association for the Advancement of Science	
	C6	EDWARDS, D.A. et al., "Recent advances in pulmonary drug delivery using large, porous inhaled particles", J. Appl. Physoil., August 1998, Pages 379-385, Vol. 85, No. 2, American Physiological Society	
	C7	ENRIQUEZ-HARRIS, P. et al., "Growth factors and the extracellular matrix", Meeting Report. Trends in Cell Biology, 1994, 2 Pages	
	C8	ERNST, S. et al., "Direct evidence for a predominantly exolytic processive mechanism for depolymerization of heparin-ike glycosaminoglycans by heparinase P", <i>Proc. Natl. Acad. Sci. USA</i> , April 1998, Pages 4182-4187, Vol. 95	
·	C9	FEINGOLD, D.S. et al., "Conformational aspects of the reaction mechanisms of polysaccharide lyases and epimerases", FEB Letters, November 1987, Pages 207-211, Vol. 223, No. 2, Elsevier Science Publishers B.V.	

J90 3 0 2002

( JAN 3 0 2002	<del>2</del> /	긁		
C10	ODAVARTI, R. et al., "Heparinase I from Flavobacterium heparinum. Identification of a Critical Histidine	<b>\$</b>		20
Tanga and	Residue Essential for Catalysis as Probed by Chemical Modification and Site-Directed Mutagenesis", Biochemistry, 1996, Pages 6846-6852, Vol. 35, No. 21, American Chemical Society	H CENTER	8333	
CII	GODAVARTI, R. et al., "Heparinase III for Flavobacterium heparinum: cloning and recombinant expression in Escherichia coli", Biochem. Biophys. Res. Commun., August 23, 1996, Pages 751-758, Vol. 225, No. 3, Academic Press, Inc.	ΝĨΕ	0 1	Ĭ
C12	GODAVARTI, R. et al., "A comparative analysis of the primary sequences and characteristics of heparinases I, II, and III from Flavobacterium heparinum", Biochem. Biophys. Res. Commun., December 24, 1996, Pages 770-777, Vol. 229, No. 3, Academic Press. Inc.	1600/2900	20,02	VE
C13	HARENBERG, J. et al., "Anticoagulant effects and tissue factor pathway inhibitor after intrapulmonary low-molecular-weight heparin", Blood Coagulation and Fibrinolysis, 1996, Pages 477-482, Vol. 7, Rapid Science Publishers	8		پ.
C14	HART, G.W., "Glycosylation", Current Opinion in Cell Biology, 1992, Pages 1017-1023, Vol. 4			
C15	HUANG, J.N. et al., "Low-Molecular-Weight Heparins", Hematology/Oncology Clinics of North America, December 1998, Pages 1251-1281, Vol. 12, No. 6			_
C16	JACKSON, R.L. et al., "Glycosaminoglycans: Molecular Properties, Protein Interactions, and Role in Physiological Processes", Physiological Reviews, April 1991, Pages 481-539, Vol. 71, No. 2, The American Physiological Society		2002	300/290
C17	KAKKAR, A.K. et al., "Venous thromboembolism and cancer", Baillier's Clinical Haematology, September 1998, Pages 675-687, Vol. 11, No. 3, Bailliere Tindall	$\stackrel{\sim}{\mathbb{L}}$	2 2	ER 16
C18	KANABROCKI, E.L. et al., "Heparin as a Therapy for Atherosclerosis: Preliminary Observations on the Intrapulmonary Administration of Low-Dose Heparin in the Moming Versus Evening Gauged by Its Effect on Blood Variables", Chronobiology International, 1991, Pages 210-233, Vol. 8, No. 3, International Society of Chronobiology	E	APR	CENTER 1600/2900
C19	KANABROCKI, E.L. et al., "A Quest for the Relief of Atherosclerosis: Potential Role of Intrapulmonary Heparin – A Hypothesis", <i>Quarterly Journal of Medicine</i> , April 1992, Pages 259-282, New Series 83, No. 300, Oxford University Press	CC		Ţ,
C20	KRETSINGER, R.H. et al., "Structure and Evolution of Calcium-Modulated Proteins", CRC Critical Reviews in Biochemistry, July 1980, Pages 119-174, Vol. 8, No. 2			
C21	LECKBAND, D. et al., "An Approach for the Stable Immobilization of Proteins", <i>Biotechnology and Bioengineering</i> , 1991, Pages 227-237, Vol. 37, John Wiley & Sons, Inc.			
C22	LINHARDT, R.J. et al., "Polysaccharide Lyases", Applied Biochemistry and Biotechnology", 1986, Pages 135-176, Vol. 12			
C23	LINHARDT, R.J. et al., "Examination of the Substrate Specificity of Heparin and Heparan Sulfate Lyases", Biochemistry, 1990, Pages 2611-2617, Vol. 29, No. 10, American Chemical Society			
C24	LINHARDT, R.J. et al., "Production and Chemical Processing of Low Molecular Weight Heparins", Seminars in Thrombosis and Hemostatis, 1999, Pages 5-16, Vol. 25, Suppl. No. 3, Thiemo Medical Publishers, Inc.			
C25	LIU, D. et al., "The Calcium-binding Sites of Heparinase I from Flavobacterium heparinum are Essential for Enzymatic Activity", The Journal of Biological Chemistry, February 12, 1999, Pages 4089-4095, Vol. 274, No. 7, The American Society for Biochemistry and Molecular Biology, Inc.			
C26	LIU, J. et al., "Heparan Sulfate D-Glucosaminyl 3-0-Sulfotransferase-3A Sulfates N-Unsubstituted Glucosamine Residues", The Journal of Biological Chemistry, December 31, 1999, Pages 38155-38162, Vol. 274, No. 53, The American Society for Biochemistry and Molecular Biology, 1			
C27	LOHSE, D.L. et al., "Purification and Characterization of Heparin Lyases from Flavobacterium heparinum", The Journal of Biological Chemistry, December 5, 1992, Pages 24347-24355, Vol. 267, No. 34, The American Society for Biochemistry and Molecular Biology, Inc.			
C28	LUSTIG, F. et al., "Alternative Splicing Determines the Binding of Platelet-Derived Growth Factor (PDGF-AA) to Glycosaminoglycans", Biochemistry, 1996, Pages 12077-12085, Vol. 35, No. 37, American Chemical Society			
C29	POJASEK, K. et al., "Histidine 295 and histidine 510 are crucial for the enzymatic degradation of heparan sulfate by heparinase III", Biochemistry, April 11, 2000, Pages 4012-4019, Vol. 39, No. 14, American Chemistry Society			
C31	RHOMBERG, A.J. et al., "Mass spectrometric and capillary electrophoretic investigation of the enzymatic degradation of heparin-like glycosaminoglycans", <i>Proc. Natl. Acad. Sci. USA</i> , April 1998, Pages 4176-4181, Vol. 95			
C31	vol. 93  RHOMBERG, A.J. et al., "Mass spectrometric evidence for the enzymatic mechanism of the depolymerization of heparin-like glycosaminoglycans by heparinase II", Proc. Natl. Acad. Sci. USA, October 1998, Pages 12232-12237, Vol. 92  22237, Vol. 92			
C32	12237, vol. 33  SASISEKHARAN, R. et al., "Cloning and expression of heparinase I gene from Flavobacterium heparinum",  Proc. Natl. Acad. Sci. USA, April 1993, Pages 3660-3664, Vol. 90, Applied Biological Sciences			

	/ mm.		오	
	C33	SASUS HARAN, R. et al., "Heparinase inhibits neovascularization", Proc. Natl. Acad. Sci. USA, February Pages 1524-1528, Vol. 91	CEN	ΕB
•	C34	SASISEKHARAN, R. et al., "Heparinase I from Flavobacterium heparinum: The Role of the Cysteine Residue in Catalysis as Probed by Chemical Modification and Site-Directed Mutagenesis", Biochemistry, 1995, Pages 14441-14448, Vol. 34, No. 44, American Chemical Society	ER 16	012
1	C35	SASISEKHARAN, R. et al., "Heparinase I from Flavobacterium heparinum, Mapping and Characterization of the Heparin Binding Domain", The Journal of Biological Chemistry, February 9, 1996, Pages 3124-3131, Vol. 271, No. 6, The American Society for Biochemistry and Molecular Biology, Inc.	CENTER 1600/2900	2002
	C36	SASISEKHARAN, R. et al., "Heparin and heparan sulfate: biosynthesis, structure and function", Curr. Opin. Chem. Biol., December 2000, Pages 626-631, Vol. 4, No. 6, The American Society for Biochemistry and Molecular Biology, Inc.	-0	
	C37	SHRIVER, Z. et al., "Heparinase II from Flavobacter/um heparimm, Role of Histidine Residues in Enzymatic Activity as Probed by Chemical Modification and Site-Directed Mutagenesis", The Journal of Biological Chemistry, April 24, 1998, Pages 10160-10167, Vol. 273, No. 17, The American Society for Biochemistry and Molecular Biology, Inc.		
	C38	SHRIVER, Z. et al., "Heparinase II from Flavobacterium heparinum, Role of cysteine in Enzymatic Activity as Probed by Chemical Modification and Site-Directed Mutagenesis," The Journal of Biological Chemistry, September 4, 1998, Pages 22904-22912, Vol. 273, No. 36, The American Society for Biochemistry and Molecular Biology, Inc.		
	C39	SHRIVER, Z. et al., "Biochemical Investigations and Mapping of the Calcium-binding Sites of Heparinase I from Flavobacterium heparinum", The Journal of Biological Chemistry, February 12, 1999, Pages 4082-4088, Vol. 274, No. 7, The American Society for Biochemistry and Molecular Biology, Inc.		
	C40	SHRIVER, Z. et al., "Sequencing of 3-0 sulfate containing heparin decasaccharides with a partial antithrombin III binding site", <i>Proc. Natl. Acad. Sci. USA</i> , September 12, 2000, Pages 10359-10364, Vol. 97, No. 19		
	C41	SHRIVER, Z. et al., "Cleavage of the antithrombin III binding site in heparin by heparinases and its implication in the generation of low molecular weight heparin", <i>Proc. Natl. Acad. Sci. USA</i> , September 12, 2000, Pages 10365-10370, Vol. 97, No. 19		
	C42	VALENTINE, K.A. et al., "Low-Molecular-Weight Heparin Therapy and Mortality", Seminars in Thrombosis and Hemostatis, 1997, Pages 173-178, Vol. 23, No. 2, Thieme Medical Publishers, Inc.		
Ì	C43	VENKATARAMAN, G. et al., "Sequencing complex polysaccharides", Science, October 15, 1999, Pages 537-542, Vol. 286(5439)		
	C44	YANG, V.C. et al. "Purification and Characterization of Heparinase from Flavobacterium heparinum", The Journal of Biological Chemistry, February 10, 1985, Pages 1849-1857, Vol. 260, No. 3, The American Society of Biological Chemists, Inc.		
I	C45	ZACHARSKI, L.R. et al., "Blood Coagulation Activation in Cancer: Challenges for Cancer Treatment",  Hamostaseologic, 1995, Pages 14-20, Vol. 15, F.K. Schattauer Verlagsgesellschaft mbH		

EXAMINER	DATE CONSIDERED	
/Traviss Mcintosh III/ (08/14/2009)	08/14/2009	

#EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant,

\*a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application. Serial No. relied upon for an earlier filing date under 35 U.S.C. 120 (continuation, continuation-in-part, and divisional applications).

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